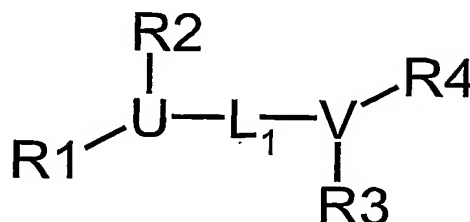


Claims:

1. A method for preventing or treating anthrax infections by inhibiting Anthrax Lethal Factor activity comprising administering a compound of the formula:



wherein U and V are, independently, C, N, or C(CH₃), L₁ is a linker and R₁, R₂, R₃ and R₄ are each independently selected substituent groups, as follows:

R₁ is Z(CHR₅)_nY where n is 0 to 4,

Z is a bond, S, CO, O, SO, SO₂, NH, NR₁₁, SO₂NR₁₁, NR₁₁SO₂, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 1,2-cyclohexylidene;

Y is a group known to bind to zinc, including CONR₁₁OH, COOH, SH, ArSH, NHCOCH₂SH, 2-hydroxybenzoate (linked at the 3,4,5, or 6-position), 2-hydroxypyridinecarboxylate (linked at the 3,4,5, or 6-position, with the ring nitrogen at any unsubstituted position), CF₂P=O(OH)₂, C(CH₃)=NOCH₂COOH, C(CH₂OH)=NOCH₂COOH, NHCO(CHR₁₁)_mSH (where m = 1 to 4), PO(OH)₂, PO(R₁₁)OH, SO₂NR₁₁OH, or NH(OH)COR₁₁, or is derivatized to form a prodrug that is capable of undergoing conversion to a zinc-binding moiety,

R₅ and R₁₁ are, independently, H, CH₃, amino, hydroxy, alkoxy, alkylthio, alkyl (C₂-C₁₀), branched alkyl (C₃-C₁₀), alkylthio (C₁-C₇), alkylthioalkyl (C₂-C₈), arylthio,

alkylamino(C1-C7), amino, arylamino, aryl, heteroaryl, arylalkyl, heterarylalkyl, arylalkenyl, heterarylalkenyl, arylalkynyl, or heterarylalkynyl,

and where **R1** can be further substituted with one or more of the following: NH_2 , OH, halogen, alkyl, CONH_2 , CONHOH , C(NH)NH_2 , C(NH)NHOH , NHC(NH)NH_2 , CN, NO_2 , NR_6R_7 where **R6** and **R7** are H or alkyl and optionally form a ring, or **R5** can form a ring with **R2** or with **R11**;

R2 is H, isobutyl, n-butyl, pentyl, methyl, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl, cycloalkylmethyl (C3-C9 cycle), $\text{Ar}(\text{CH}_2)_n$ (where n is 0 to 4, Ar is phenyl, aryl, heteroaryl), phenethyl, arylalkenyl, heterarylalkenyl, arylalkynyl, heterarylalkynyl, alkenyl (C2-C8), alkynyl (C2-C8), pentafluorophenoxyethyl, pentafluorophenylmethyl, cycloalkenyl (C4-C10), alkylthio, arylthio, alkylamino, arylamino, aryl, dichlorophenyl, or **R2** can form a ring with **R5**, **R11**, **L1**, or **R3**, and **R5** and **R11** can be substituted with one or more of the following: NH_2 , OH, halogen, alkyl, CF_3 , CF_3O , CF_3S , alkoxy, alkylthio, SO_2alkyl (C1-C4), CONH_2 , CONHOH , C(NH)NH_2 , CN, NO_2 , C(NH)NHOH , NHC(NH)NH_2 , or NR_6R_7 where **R6** and **R7** are H or alkyl and can form a ring;

R3 is H, phenethyl, alkyl (C1-C10), branched alkyl (C1-C10), aryl, phenyl substituted with aryl or heteroaryl at the 2-, 3-, or 4-positions, benzyloxy, pyrrolyl substituted with 1-2 aryl groups, 2-aryl-1,3,4 thiadiazolyl, heteroaryl (including thiophenyl), $-\text{L2Ar}$ where Ar includes 1-naphthyl, 2-naphthyl, 4-phenylphenyl, 5-(2-thienyl)-2-thienyl, 4-(3'-methoxyphenyl)phenyl, 4-(4'-methoxyphenyl)phenyl, 3-indolyl, phenyl, t-butyl, indolyl 3-phenylphenyl, indolyl, 2,3-dimethyl-5-indolyl, benzothiophenyl, 4-(1,2,3-thiadiazol-4-yl)phenyl, 4-(2-thienyl)phenyl, 5-(2-pyridyl)-2-thienyl, 1-(2-naphthyl)vinylaminoalkyl, N-hydroxybenzamidin-4-yl, 2-methylcarbazol-3-yl, 2-ethylcarbazol-3-yl, aryl or heteroaryl and **L2** is a linker chosen from the following, in both orientations: bond, CH_2 , $(\text{CH}_2)_2$, CH_2NHCH_2 , $\text{CH}_2\text{CH}_2\text{CONHCH}_2$, $\text{CH}_2\text{CH}_2\text{CONHCH}_2\text{CH}_2$, 1,1 vinylidene, 1,2-vinylidene, CO, $\text{CH}_2\text{CH}_2\text{NHCH}_2$, $\text{CH}_2\text{CH}_2\text{CH}_2\text{NHCH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2$, $(\text{CH}_2)_q$ where q = 3 to 7, $(\text{CHR}_9)_r$ where r = 1 to 7 and **R9** is independently H, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl (C3-C10), cycloalkylalkyl (C4-C14), alkyl thio, amino, alkyl amino, dialkylamino,

(CHR⁹)_sX(CHR⁹)_t where $s + t = 0$ to 8, X is O, S, CO, SO, SO₂, NH, CONH, NHCO, SO₂NH, NHSO₂ or NR⁹ and R⁹ is independently H, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl (C3-C10), cycloalkylalkyl (C4-C14), acyl, alkyl thio, amino, alkyl amino, or dialkylamino, and R⁹ also includes N-linked heterocycles such as piperidine, pyrroline, (1,2,3,4-)tetrahydrobetacarbolin-2yl, R¹⁵ is H, alkyl (C1-C4), branched alkyl (C3-C5), or cycloalkyl(C3-C5), carbon-carbon single bonds in R⁸ can optionally be substituted with double or triple bonds, and where R³ can form a ring with R², L¹, or R⁴, or R³, R⁹ and R¹⁵ are further substituted with one or more of the following NH₂, OH, halogen, N(CH₃)₂, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, CONH₂, CONHOH, C(NH)NH₂, CN, NO₂, C(NH)NHOH, NHC(NH)NH₂, aryloxy, trifluoromethylphenoxy, carboxyalkyl (C2-C8), (Carboxyphenyl)methylthio, carboxyalkylthio (C2-C8), carboxyphenyl, NR⁶R⁷ where R⁶ and R⁷ are H or alkyl or can form a ring;

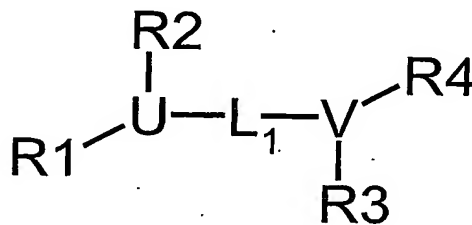
R⁴ is H, alkyl (C1-C10), branched alkyl (C1-C10), arylalkyl, heteroarylalkyl, CONR¹⁰R¹⁶ where R¹⁰ is H, methyl, alkyl (C2-C10), branched alkyl (C3-C10), benzyl, phenethyl, arylalkyl, heteroarylalkyl, alkanoyl (C2-C8), branched alkanoyl, aroyl (C6-C12), heteroaroyl (C2-C10), isopropyl, CONR¹⁶R¹²; and where R¹² and R¹⁶ are, independently, H, methyl, alkyl, benzyl, 2-phenylethyl, 2-indanyl, 2-morpholinylethyl, (2,6)-dimethoxybenzyl, dimethylaminoethyl, (2-pyridyl)methyl, 2-(2-pyridyl)ethyl, 4-carboxybenzyl, 1-phenylethyl, CH(CONH₂)CH₂C₆H₅, CH(CONH₂)CH₂CH(CH₃)₂, CH(CONH₂)CH(CH₃)CH₂CH₃, CH(CONH₂)CHCH₃, CH(CH₂OCH₃)CH₂C₆H₅, CH(CONHCH₂CH₂OCH₃)CH₂cyclohexyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, aminoalkyl, hydroxyalkyl, (trifluoromethylphenoxy)phenyl. NR¹⁶R¹² can optionally form an N-linked monocyclic or bicyclic heterocyclic ring, including but not limited to 1,2-dihydroisoindole, octahydroisoindole, morpholine, piperidine, piperazine, N-alkyl piperazine (C1-C4), homopiperazine, 3-pyrroline, pyrrolidine, tetrahydroisoquinoline, octahydropyrrolo[3,4-C]pyrrole, L-proline, L-proline dimethylamide, D-proline, D-proline dimethylamide, and thiazolidine, or

R⁴ can form a ring with L¹ or R³, and R⁴, R⁶, R⁷, R¹⁰, R¹¹, R¹² and R¹⁶ can be further substituted, independently, with 1 to 3 of the following substituents: NH₂, OH, F, Cl, Br, methyl, alkyl, aryl, cycloalkyl (C3-C6), heterocycloalkyl, heteroaryl, CF₃,

CF₃O, CF₃S, CF₃, aryloxy, trifluoromethylphenoxy, alkoxy, alkylthio, CONH₂, CN, NO₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR₆R₇ where R₆ and R₇ are H or alkyl, or can form a ring; and

L1 is a linker including the following, in either orientation: single bond, double bond, CONH, NHCO, N(CH₃)CO, CON(CH₃), CH₂NH, NHCH₂, CH=CH, C(NH₂)=N, N=C(NH₂), arylene (linked 1,2-; 1,3-; or 1,4), heteroarylene (linked 1,2-; 1,3-; or 1,4), ethynyl, CH=CF, CF=CH, CF=CF, CH₂CH₂, C(CH₃)=CH, CH=C(CH₃), SO₂NH, SO₂, COCH₂, CH₂CO, CNOHCH₂, CH₂CNOH, C(CF₃)=CH, CH=C(CF₃), SO₂CH₂, CH₂SO₂, SOCH₂, CH₂SO, CH₂CHOH, CHOHCH₂, lower cycloalkyl (C3-C6), or CHOHCHOH, or where L1 can be substituted with one or more of the following: NH₂, OH, halogen, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, CONH₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR₆R₇ where R₆ and R₇ are H or alkyl and optionally form a ring.

2. A pharmaceutical composition useful for preventing or treating anthrax infections by inhibiting Anthrax Lethal Factor activity comprising a compound of the formula:



wherein U and V are, independently, C, N, or C(CH₃), L₁ is a linker and R₁, R₂, R₃ and R₄ are each independently selected substituent groups, as follows:

R₁ is Z(CHR₅)_nY where n is 0 to 4,

Z is a bond, S, CO, O, SO, SO₂, NH, NR₁₁, SO₂NR₁₁, NR₁₁SO₂, 1,2-phenylene, 1,3-phenylene, 1,4-phenylene, 1,2-cyclohexylidene;

Y is a group known to bind to zinc, including CONR₁₁OH, COOH, SH, ArSH, NHCOCH₂SH, 2-hydroxybenzoate (linked at the 3,4,5, or 6-position), 2-hydroxypyridinecarboxylate (linked at the 3,4,5, or 6-position, with the ring nitrogen at any unsubstituted position), CF₂P=O(OH)₂, C(CH₃)=NOCH₂COOH, C(CH₂OH)=NOCH₂COOH, NHCO(CHR₁₁)_mSH (where m = 1 to 4), PO(OH)₂, PO(R₁₁)OH, SO₂NR₁₁OH, or NH(OH)COR₁₁, or is derivatized to form a prodrug that is capable of undergoing conversion to a zinc-binding moiety,

R5 and **R11** are, independently, H, CH₃, amino, hydroxy, alkoxy, alkylthio, alkyl (C2-C10), branched alkyl (C3-C10), alkylthio (C1-C7), alkylthioalkyl (C2-C8), arylthio, alkylamino (C1-C7), amino, arylamino, aryl, heteroaryl, arylalkyl, heterarylalkyl, arylalkenyl, heterarylalkenyl, arylalkynyl, or heterarylalkynyl,

and where **R1** can be further substituted with one or more of the following: NH₂, OH, halogen, alkyl, CONH₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, CN, NO₂, NR₆R₇ where **R6** and **R7** are H or alkyl and optionally form a ring, or **R5** can form a ring with **R2** or with **R11**;

R2 is H, isobutyl, n-butyl, pentyl, methyl, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl, cycloalkylmethyl (C3-C9 cycle), Ar(CH₂)_n (where n is 0 to 4, Ar is phenyl, aryl, heteroaryl), phenethyl, arylalkenyl, heterarylalkenyl, arylalkynyl, heterarylalkynyl, alkenyl (C2-C8), alkynyl (C2-C8), pentafluorophenoxyethyl, pentafluorophenylmethyl, cycloalkenyl (C4-C10), alkylthio, arylthio, alkylamino, arylamino, aryl, dichlorophenyl, or **R2** can form a ring with **R5**, **R11**, **L1**, or **R3**, and **R2**, **R5** and **R11** can be substituted with one or more of the following: NH₂, OH, halogen, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, SO₂alkyl (C1-C4), CONH₂, CONHOH, C(NH)NH₂, CN, NO₂, C(NH)NHOH, NHC(NH)NH₂, or NR₆R₇ where **R6** and **R7** are H or alkyl and can form a ring;

R3 is H, phenethyl, alkyl (C1-C10), branched alkyl (C1-C10), aryl, phenyl substituted with aryl or heteroaryl at the 2-, 3-, or 4-positions, benzyloxy, pyrrolyl substituted with 1-2 aryl groups, 2-aryl-1,3,4 thiadiazolyl, heteroaryl (including thiophenyl), -**L2Ar** where **Ar** includes 1-naphthyl, 2-naphthyl, 4-phenylphenyl, 5-(2-thienyl)-2-thienyl, 4-(3'-methoxyphenyl)phenyl, 4-(4'-methoxyphenyl)phenyl, 3-indolyl, phenyl, t-butyl, indolyl, 3-phenylphenyl, indolyl, 2,3-dimethyl-5-indolyl, benzothiophenyl, 4-(1,2,3-thiadiazol-4-yl)phenyl, 4-(2-thienyl)phenyl, 5-(2-pyridyl)-2-thienyl, 1-(2-naphthyl)vinylaminoalkyl, N-hydroxybenzamidin-4-yl, 2-methylcarbazol-3-yl, 2-ethylcarbazol-3-yl, aryl or heteroaryl and **L2** is a linker chosen from the following, in both orientations: bond, CH_2 , $(\text{CH}_2)_2$, CH_2NHCH_2 , $\text{CH}_2\text{CH}_2\text{CONHCH}_2$, $\text{CH}_2\text{CH}_2\text{CONHCH}_2\text{CH}_2$, 1,1 vinylidene, 1,2-vinylidene, CO, $\text{CH}_2\text{CH}_2\text{NHCH}_2$, $\text{CH}_2\text{CH}_2\text{CH}_2\text{NHCH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2$, $(\text{CH}_2)_q$ where $q = 3$ to 7 , $(\text{CHR}9)_r$ where $r = 1$ to 7 and **R9** is independently H, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl (C3-C10), cycloalkylalkyl (C4-C14), alkyl thio, amino, alkyl amino, dialkylamino, $(\text{CHR}9)_s\text{X}(\text{CHR}9)_t$ where $s + t = 0$ to 8 , **X** is O, S, CO, SO, SO_2 , NH, CONH, NHCO, SO_2NH , NHSO_2 or **NR9** and **R9** is independently H, alkyl (C1-C10), branched alkyl (C3-C10), cycloalkyl (C3-C10), cycloalkylalkyl (C4-C14), acyl, alkyl thio, amino, alkyl amino, or dialkylamino, and **R9** also includes N-linked heterocycles such as piperidine, pyrroline, (1,2,3,4-)tetrahydrobetacarbolin-2yl, **R15** is H, alkyl (C1-C4), branched alkyl (C3-C5), or cycloalkyl(C3-C5), carbon-carbon single bonds in **R8** can optionally be substituted with double or triple bonds, and where **R3** can form a ring with **R2**, **L1**, or **R4**, or **R3**, **R9** and **R15** are further substituted with one or more of the following NH_2 , OH, halogen, $\text{N}(\text{CH}_3)_2$, alkyl, CF_3 , CF_3O , CF_3S , alkoxy, alkylthio, CONH_2 , CONHOH , $\text{C}(\text{NH})\text{NH}_2$, CN, NO_2 , $\text{C}(\text{NH})\text{NHOH}$, $\text{NHC}(\text{NH})\text{NH}_2$, aryloxy, trifluoromethylphenyloxy, carboxyalkyl (C2-C8), (Carboxyphenyl)methylthio, carboxyalkylthio (C2-C8), carboxyphenyl, **NR6R7** where **R6** and **R7** are H or alkyl or can form a ring;

R4 is H, alkyl (C1-C10), branched alkyl (C1-C10), arylalkyl, heteroarylalkyl, **CONR10R16** where **R10** is H, methyl, alkyl (C2-C10), branched alkyl (C3-C10), benzyl, phenethyl, arylalkyl, heteroarylalkyl, alkanoyl (C2-C8), branched alkanoyl, aroyl (C6-

C12), heteroaroyl (C2-C10), isopropyl, CONR16R12; and where R12 and R16 are, independently, H, methyl, alkyl, benzyl, 2-phenylethyl, 2-indanyl, 2-morpholinylethyl, (2,6)-dimethoxybenzyl, dimethylaminoethyl, (2-pyridyl)methyl, 2-(2-pyridyl)ethyl, 4-carboxybenzyl, 1-phenylethyl, CH(CONH₂)CH₂C₆H₅, CH(CONH₂)CH₂CH(CH₃)₂, CH(CONH₂)CH(CH₃)CH₂CH₃, CH(CONH₂)CHCH₃, CH(CH₂OCH₃)CH₂C₆H₅, CH(CONHCH₂CH₂OCH₃)CH₂cyclohexyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, aminoalkyl, hydroxyalkyl, (trifluoromethylphenoxy)phenyl. NR16R12 can optionally form an N-linked monocyclic or bicyclic heterocyclic ring, including but not limited to 1,2-dihydroisoindole, octahydroisoindole, morpholine, piperidine, piperazine, N-alkyl piperazine (C1-C4), homopiperazine, 3-pyrroline, pyrrolidine, tetrahydroisoquinoline, octahydropyrrolo[3,4-C]pyrrole, L-proline, L-proline dimethylamide, D-proline, D-proline dimethylamide, and thiazolidine, or

R4 can form a ring with L1 or R3, and R4, R6, R7, R10, R11, R12 and R16 can be further substituted, independently, with 1 to 3 of the following substituents: NH₂, OH, F, Cl, Br, methyl, alkyl, aryl, cycloalkyl (C3-C6), heterocycloalkyl, heteroaryl, CF₃, CF₃O, CF₃S, CF₃, aryloxy, trifluoromethylphenoxy, alkoxy, alkylthio, CONH₂, CN, NO₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR6R7 where R6 and R7 are H or alkyl, or can form a ring; and

L1 is a linker including the following, in either orientation: single bond, double bond, CONH, NHCO, N(CH₃)CO, CON(CH₃), CH₂NH, NHCH₂, CH=CH, C(NH₂)=N, N=C(NH₂), arylene (linked 1,2-; 1,3-; or 1,4), heteroarylene (linked 1,2-; 1,3-; or 1,4), ethynyl, CH=CF, CF=CH, CF=CF, CH₂CH₂, C(CH₃)=CH, CH=C(CH₃), SO₂NH, SO₂, COCH₂, CH₂CO, CNOHCH₂, CH₂CNOH, C(CF₃)=CH, CH=C(CF₃), SO₂CH₂, CH₂SO₂, SOCH₂, CH₂SO, CH₂CHOH, CHOHCH₂, lower cycloalkyl (C3-C6), or CHOHCHOH, or where L1 can be substituted with one or more of the following: NH₂, OH, halogen, alkyl, CF₃, CF₃O, CF₃S, alkoxy, alkylthio, CONH₂, CONHOH, C(NH)NH₂, C(NH)NHOH, NHC(NH)NH₂, NR6R7 where R6 and R7 are H or alkyl and optionally form a ring, together with a pharmaceutically acceptable carrier.